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Physical activity and the risk of colon cancer among women: A prospective cohort study (United States)

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KEYWORDS

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ABSTRACT

Physical activity has frequently been reported to decrease the risk of colon cancer in men, but data on the relation of physical activity to colon cancer risk in women have generally been less consistent. To further investigate the relationship of physical activity with colon cancer risk in women, we studied a cohort of 31,783 US women participating in the Breast Cancer Detection Demonstration Project Follow-up Study. Information on daily physical activity over the past year was ascertained using a self-administered questionnaire at study baseline. The Cox proportional hazards model was used to estimate relative risks (RRs) relating physical activity to the risk of incident colon cancer. During 270,325 person-years of follow-up, 243 colon cancer cases were identified. No association was observed between physical activity and the subsequent risk of colon cancer. The multivariable RRs of colon cancer across increasing quintiles of total physical activity were 1.0, 1.45, 1.16, 1.27 and 1.15 (95% CI: 0.76, 1.75; p_{trend} = 0.77). The multivariable RRs comparing women at the extremes of moderate and vigorous physical activity, respectively, were 1.07 (95% CI: 0.70, 1.62) and 1.10 (95% CI: 0.78, 1.55). The relationship between physical activity and colon cancer risk did not vary by anatomic subsite or across subgroups defined by age, body mass, dietary fiber intake, menopausal status, menopausal hormone use or aspirin use. The results of this large prospective cohort study among women do not support the hypothesis that physical activity is related to a lower incidence of colon cancer. © 2006 Wiley-Liss, Inc.

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ARTICLE TEXT

Background

Colon cancer, the 3rd most common cancer among women in the United States (excluding nonmelanoma skin cancer), accounts for roughly 57,000 new cancer diagnoses each year.[1] Epidemiologic evidence suggests that one-half to two-thirds of all colon cancers could be prevented by maintaining a healthy body weight, diet and lifestyle.[2][3][4][5]

Over 40 epidemiologic studies have examined the association between physical activity and the risk of developing colon cancer.[6][7] Using both cohort and case-control study designs,[8][9][10] many of these studies have observed a reduction in the risk of colon cancer, comparing individuals at the extremes of recreational, occupational or total physical activity.[8][11] Intriguingly, several studies have observed a stronger inverse association between physical activity and colon cancer risk in men than in women,[12][13][14][15][16][17][18][19] and a number of studies have reported an apparent inverse association in men but no association in women.[14][19][20][21][22][23][24]

Specifically, 6[17][21][25][26][27][28] of 16 prospective studies[17][19][20][21][23][25][26][27][28][29][30][31][32][33][34][35] on physical activity and colon cancer in women have reported a statistically significant reduction in the risk of colon cancer with increased levels of recreational, occupational or total physical activity. In addition, one study detected a 50% reduction in the risk of colon cancer with increasing levels of recreational physical activity that did not reach statistical significance.[31] Eight of the nine remaining studies reported nonsignificant relative risks (RRs) ranging from 0.8 to 1.2.[19][20][23][30][32][33][34][35] The final study observed a statistically non-significant 40% increase in colon cancer risk for nonrecreational activity.[29] Thus, the relationship between physical activity and colon cancer risk in women is not entirely consistent.

One possible reason for the variation in findings from previous studies of physical activity and colon cancer in women is the potential for imprecision related to the measurement of physical activity.[36] Studies that have specifically inquired about the amount of time spent at individual activities[25][28] have tended to observe stronger reductions in colon cancer risk than studies that have used 1 or 2 broad questions encompassing all activities.[23][31] Another possibility is the methodologically greater challenge in measuring physical activity in women as compared to that in men. For example, household activity may be of particular significance in women [37] and has been included in few analyses of physical activity and colon cancer risk to date.[38]

In addition to heterogeneity across previous studies on the association between physical activity and colon cancer risk in women, the magnitude of specific dimensions of physical activity that might reduce colon cancer risk, such as activity frequency, intensity and duration, have yet to be elucidated.[6][7][11] The present analysis, which accounts for activity intensity and duration, was undertaken to further examine the relationship between physical activity and colon cancer risk in a large cohort of women.

Material and methods

The BCDDP cohort

In 1973, 283,222 women were enrolled in the Breast Cancer Detection Demonstration Project (BCDDP), a program jointly sponsored by the American Cancer Society and the National Cancer Institute.[39] Between 1973 and 1980, BCDDP participants were screened for breast cancer at 29 screening centers throughout 27 US cities. From this initial cohort, the National Cancer Institute selected 64,182 women to take part in the BCDDP Follow-up Study. This cohort, initiated in 1979-1980, included all women with biopsies indicating benign breast disease (n = 25,114), all women recommended for biopsies or surgery who did not undergo the procedure (n = 9,628), all women diagnosed with breast cancer during the screening program (n = 4,275) and, finally, a sample of women who neither underwent nor were recommended for breast biopsy and who were matched to the above women on age, time of entry into the screening program, length of participation, ethnicity and screening center (n = 25,165).

The BCDDP Follow-up Study was completed in 4 phases. The first phase began in 1979-1980 with the return of a baseline questionnaire, and continued with up to 6 (usually 4) annual telephone interviews. Phases II, III and IV took place during 1987-1989, 1993-1995 and 1995-1998, respectively, and each included a mailed follow-up

questionnaire. These questionnaires were designed to update participants' exposures to selected risk-factors and to identify new cancer diagnoses.

Population for analysis

Of the 64,182 participants in the follow-up study, 61,430 (96%) completed the baseline questionnaire. Of these women, 51,691 completed the phase II questionnaire, which collected information on physical activity. We excluded 6,660 women who were diagnosed with cancer (other than nonmelanoma skin cancer) prior to the beginning of follow-up in 1987 and 3 women whose recorded entry into the cohort occurred after their recorded exit date. Also excluded from the analysis were women with missing or extreme (greater than 3,800 or below 400 kcal/day) values of total energy intake (n = 2,773), missing or extreme (greater than 3 standard deviations above or below the mean) values of body mass index (BMI; n = 3,364) and women for whom a physical activity index (PAI) could not be calculated due to inadequate information on physical activity (n = 7,108).

A total of 31,783 participants were included in the final analytic cohort. Of these participants, 27,796 (87%) completed the phase III questionnaire, 26,919 (85%) completed the phase IV questionnaire and 28,958 (91%) completed either the phase III or phase IV questionnaire. The majority of participants in the analytic cohort were white (89%), while a small percentage were African American (5%), Asian American (3%), Hispanic (2%) or of missing race/ethnicity (1%). The vast majority of participants (92%) were postmenopausal at baseline. The participants in the final analysis were similar to the women excluded from the analytic cohort with respect to age, level of education, race, smoking status and family history of colon cancer. Women excluded from the analytic cohort were somewhat less likely to have graduated from high school (40% *vs.* 49%) than women included in the cohort.

Identification of cases

During follow-up, 147 cases of colon cancer were identified by self-report. Of these 147 self-reported cancers, 136 (93%) were confirmed by pathology reports, data from state cancer registries, or both. Given this high confirmation rate of self-reported cancers, the 11 unconfirmed colon cancer cases were included in the final analysis. Cases ascertained by searching the National Death Index for death certificates indicating a diagnosis of colon cancer during the follow-up period were also included in the analysis (n = 62). Lastly, 34 colon cancer cases, not identified by self-report or the National Death Index, but rather, indicated on pathology reports or state cancer registries, were included in the analysis, resulting in a total of 243 colon cancer cases available for the final analysis. Excluding the 11 unconfirmed, self-reported cancers and 34 cancers identified by methods other than self-report or death certificate did not materially affect the results. Thus, all cases of colon cancer were included in the present analysis.

Physical activity assessment

The phase II questionnaire asked participants to report their normal weekday and weekend activity over the past year. Specifically, participants were asked to estimate the number of hours they spent per day sleeping and engaging in light, moderate and vigorous activities, and to sum these 4 categories to equal 24 hr. Examples provided of light activity included sitting, working in an office, watching TV and driving a car. Examples of moderate activity included light housework, hiking and golf. Heavy housework, strenuous sports/exercise and aerobics were given as examples of vigorous activity. Plausible ranges for physical activity were established using a set of predefined standards. These ranges were: 4-18 hr for sleep, 0-20 hr for light activity, 0-18 hr for moderate activity and 0-18 hr for vigorous activity. For a participant's 24-hr estimate to be considered valid, sleep had to be within the acceptable range of 4-18 hr and light, moderate and vigorous activity estimates had to fall in the plausible range or left blank (in which case a value of zero was assumed). As mentioned previously, participants whose activity data was deemed implausible or who did not provide information on activity were excluded from the study population.

The reported number of hours spent sleeping and engaged in light, moderate and vigorous activities on a typical weekday and weekend day were weighted to equal 24 hr. These values were used to create a PAI based on the metabolic equivalent task (MET) specific to each activity intensity level (one MET is defined as the energy expended while sitting quietly, equal to 3.5 ml O_2/kg/min).[40] For both weekday and weekend physical activity estimates, the following formula was used to calculate the PAI for a typical day:

PAI for a usual day = (hours of sleep × 1) + (hours of light physical activity × 2) + (hours of moderate physical activity × 4) + (hours of vigorous physical activity × 6)

In addition, a weighted PAI index that incorporated the PAI estimates for both weekday and weekend activity was calculated to estimate average total activity per day, expressed in MET units. The following formula was

used to calculate the weighted PAI index:

PAI = ((weekday PAI × 5) + (weekend day PAI × 2))/7

To account for intensity of physical activity, we also considered moderate and vigorous activities as individual measures of physical activity. In addition, the following question was also posed to participants in the phase II questionnaire: "At least once a week, do you engage in any regular activity similar to brisk walking, bicycling, etc., long enough to work up a sweat?". Participants were also asked to report the number of times per week they engaged in physical activity to the point of sweating.

Although our physical activity measure has not been directly compared with activity diaries or other validation instruments, our instrument closely resembles the one used in the Framingham Heart Study, which showed a correlation between physical activity reported on the questionnaire and that from indirect calorimetry of 0.43.[41] Our instrument contains important elements of the College Alumnus Physical Activity Questionnaire (PAI-CAQ),[42] an instrument that has been shown to be correlated with maximum oxygen uptake, percentage body fat, high-density lipoprotein levels and BMI.[43][44] In addition, our physical activity questions predict cardiovascular mortality among women in our cohort (data not shown).

Statistical analysis

Hazard ratios of colon cancer were computed to estimate RRs and 95% confidence intervals using Cox proportional hazards regression. Person-years of follow-up were used as the underlying time metric, calculated as the number of years between the date of completion of the phase II questionnaire to study exit date. The completion date (1987-1989) of the phase II questionnaire marked the beginning of follow-up for the current study. Women contributed person-time until the earliest of the following dates: colon cancer diagnosis, death from any cause, completion of the phase IV questionnaire or the end of study date. Because of linkage to the National Death Index and the state cancer registries, we assumed that cancer-free women not known to be dead who did not complete the phase IV questionnaire were alive and cancer free. We, therefore, assigned their end-of-study date to be the date on which they would have completed the phase IV questionnaire, based on the average interval between questionnaires from all women who completed them. Proportional hazards assumptions were evaluated by including the crossproduct term of physical activity and total follow-up time (person-years) in the models. There were no departures from the proportional hazards assumptions for total physical activity (PAI) or for the average daily hours of moderate or vigorous physical activity.

Total and moderate activities was divided into quintiles based on the distribution in the study population. The quintile ranges for total activity (as measured by the PAI index) were: 34.0-48.5, 48.51-54.3, 54.31-59.0, 59.1-64.9 and 65.0-98.1 MET-hr/day. For daily-average hours of vigorous activity, those who reported zero hours of vigorous activity were placed in one category, while the nonzero values were divided into tertiles (0.1-1, 1.1-2, 2-14 hr/day). The total number of times per week participants engaged in physical activity to the point of sweating was analyzed in categories of 0, 1-3, 4-5 and >5 times/week. Relative risks and their 95% confidence intervals were calculated with the lowest quintile or category of physical activity serving as the reference group.

Information on covariates was obtained from the phase II questionnaire. Two models were created for the analysis. In the first model, we adjusted for age at baseline (<55, 55-59.9, 60-64.9, 65-69.9, >70 years). The second model additionally contained BMI (continuous in units of kg/m^2), education (greater *vs.* less than high school), family history of colon cancer (yes, no, missing), cigarette smoking status (ever, never, unknown), menopausal hormone use (ever, never, unknown), aspirin/NSAIDS use (ever, never, unknown), alcohol consumption (drinks per day: 0, 0.01-0.50, 0.51-1.00, 1.01-2.00, >2.00) and energy-adjusted intakes of total calcium and red meat. These covariates were chosen as *a priori* covariates for inclusion in the second model. In addition, the following variables were evaluated for potential confounding: height, race, personal history of diabetes, multivitamin use and energy-adjusted total intakes of fat, fiber, vitamin D and folate. These variables did not noticeably alter the association between physical activity and colon cancer risk, and therefore were not included in the second model.

To test for linear trend across increasing categories of physical activity, the median value of each category of physical activity was entered as a single ordinal variable, the coefficient for which was evaluated by the Wald test. All *p*-values are reported by 2-sided tests. Effect modification was examined by including in the model a crossproduct interaction term between physical activity and the covariate of interest along with the main effects term. The coefficient for the crossproduct term was evaluated using the Wald test. Subsite analyses examining the association between physical activity and cancer cases of the proximal ($n = 103$) and distal ($n = 68$) colon were also performed. In analyses of distal colon cancer, we grouped physical activity into tertiles

because of low case numbers. All statistical analyses were performed using Statistical Analysis Systems (SAS) release 8.2 (SAS Institute, Cary, NC).

Results

Between 1987-1989 and 1995-1998, 243 cases of incident colon cancer were identified during 270,325 person-years of follow-up. Participant characteristics at baseline (phase II) by quintile of PAI are shown in Table I. Women with higher levels of physical activity tended to have a lower BMI and they appeared less likely to smoke, to drink alcohol or to have graduated from high school than women with lower levels of activity.

Table I. Baseline Characteristics of the BCDDP Follow-up Study Participants (*n* = 31,783) by Quintile of Total Physical Activity[1]

Characteristic	PAI quintile (MET-hr/day)				
	Q1 (34.0-48.5)	Q2 (48.51-54.3)	Q3 (54.31-59.0)	Q4 (59.1-64.9)	Q5 (65.0-98.1)
Number of participants	6,313	6,318	6,394	6,482	6,276
Mean physical activity (hr/day)					
Sleep	7.9	7.7	7.6	7.5	7.2
Light	13.9	11.2	9.0	7.2	5.0
Moderate	2.1	4.6	6.6	7.8	8.7
Vigorous	0.1	0.5	0.8	1.5	3.2
Mean age (years)	61.7	61.1	61.2	60.8	60.9
Mean height (meters)	1.6	1.6	1.6	1.6	1.6
Mean weight (kg)	67.8	66.6	66.3	65.7	65.2
Mean body mass index (kg/m^2)	25.2	24.8	24.6	24.4	24.3
Education (>high school; %)	55.0	49.7	46.7	46.6	41.2
Race (% white)	90.6	89.5	90.3	89.4	87.0
Family history of colorectal cancer (%)	11.2	11.1	12.5	11.8	11.6
Personal history of diabetes mellitus (%)	7.0	5.1	4.5	3.8	4.1
Ever smoked (%)	46.9	44.4	42.8	42.0	40.8
Aspirin/NSAID ever-use (%)	38.0	39.4	40.0	39.1	39.4
Menopausal hormone therapy (% users, Phase II)[2]	54.7	53.5	55.2	55.5	53.9
Parous (%)	84.6	86.2	86.9	84.3	88.3
Mean dietary intakes					
Energy intake (kcal/day)	1,261.6	1,264.6	1,274.7	1,279.0	1,288.7
Alcohol (>one drink/day; %)	8.5	8.2	7.5	8.0	7.1
Total fat (g/day)[3]	46.6	46.1	45.9	45.5	45.4
Dietary fiber (g/day)[3]	10.5	10.7	11.0	11.3	11.2
Red meat (g/day)[3]	83.6	84.8	85.1	84.6	86.4
Calcium (mg/day)[3,4]	1,050.8	939.0	957.3	1,017.6	945.2
Vitamin D (IU/day)[3,4]	298.3	293.0	283.2	291.2	281.0
Folate (μg/day)[3,4]	413.7	412.1	405.4	422.9	412.2

[1] All values (except age) were standardized to the age distribution of the cohort.

[2] Percentage includes both unopposed estrogen and estrogen plus progestin hormone therapy users.

[3] **Adjusted for total energy intake.**

[4] **Accounts for reported dietary intake as well as intake derived from supplements.**

No significant association between total physical activity and colon cancer risk was observed in age-adjusted analysis (Table II). After further adjustment for potential colon cancer risk-factors, the RRs across increasing quintiles of total physical activity compared to that of the lowest quintile were 1.45, 1.16, 1.27 and 1.15 (95% CI: 0.76, 1.75; $p_{trend} = 0.77$). Excluding BMI from the models or excluding the first year of follow-up did not significantly change the results.

Table II. Relative Risk (RR) of Colon Cancer in Relation to Physical Activity in the BCDDP Follow-up Study

Total physical activity[1]						*p*-trend
MET-hr/day	34.0-48.5	48.51-54.3	54.31-59.0	59.1-64.9	65.0-98.1	
Cases	44	58	47	49	45	
Person-years	52,666	53,628	54,645	55,556	53,830	
Age-adjusted RR (95% CI)	1.00	1.33 (0.90, 1.97)	1.04 (0.69, 1.58)	1.11 (0.74, 1.67)	1.04 (0.68, 1.57)	0.79
Multivariable RR (95% CI)[2]	1.00	1.45 (0.98, 2.15)	1.16 (0.77, 1.75)	1.27 (0.84, 1.91)	1.15 (0.76, 1.75)	0.77
Moderate activity[1,3]						
Hr/day	0-3.0	3.01-5.0	5.01-6.70	6.71-8.14	8.15-18.0	
Cases	45	54	60	39	45	
Person-years	53,741	56,851	52,355	53,002	54,376	
Age-adjusted RR (95% CI)	1.00	1.13 (0.76, 1.68)	1.32 (0.90, 1.94)	0.84 (0.54, 1.28)	0.97 (0.64, 1.47)	0.50
Multivariable RR (95% CI)[2,4]	1.00	1.23 (0.82, 1.83)	1.47 (0.99, 2.21)	0.94 (0.61, 1.46)	1.07 (0.70, 1.62)	0.80
Vigorous activity[5,6]						
Hr/day	0	0.1-1.0	1.1-2.0	2.1-14.0	N/A	
Cases	105	54	34	50	N/A	
Person-years	101,385	63,684	50,731	54,525	N/A	
Age-adjusted RR (95% CI)	1.00	1.02 (0.73, 1.43)	0.78 (0.53, 1.14)	0.99 (0.71, 1.39)	N/A	0.78
Multivariable RR (95% CI)[2,7]	1.00	1.19 (0.85, 1.66)	0.87 (0.59, 1.29)	1.10 (0.78, 1.55)	N/A	0.80

[1] **Categorized into quintiles.**

[2] **The multivariable model is adjusted for age, BMI, education, family history of colorectal cancer, smoking status, menopausal hormone use, aspirin use, alcohol consumption and energy-adjusted intakes of total calcium and red meat.**

[3] **On the phase II questionnaire, the following were provided as examples of moderate activity: light housework, vacuuming, washing clothes, painting, home repairs, lawn mowing, general gardening, raking, light sports or exercise, walking, hiking, light jogging, recreational tennis, bowling, golf and bicycling on level ground.**

[4] Also adjusted for vigorous activity.

[5] Vigorous physical activity: category of zero hours per day, followed by tertiles.

[6] The following were listed as examples of vigorous activity on the phase II questionnaire: heavy housework, scrubbing floors, washing windows, heavy yardwork, digging in garden, chopping wood, strenuous sports/exercise, running, fast jogging, competitive tennis, aerobics, bicycling on hills and fast dancing.

[7] Also adjusted for moderate activity.

To account for intensity of physical activity, we performed separate analyses according to quintiles of moderate activity and categories of vigorous activity. Neither moderate nor vigorous physical activity was significantly associated with colon cancer risk (Table II). The multivariable RR for the highest *versus* lowest quintile of moderate physical activity was 1.07 (95% CI: 0.70, 1.62; p_{trend} = 0.80) and for the highest *versus* lowest category of vigorous physical activity, it was 1.10 (95% CI: 0.78, 1.55; p_{trend} = 0.80). The associations between physical activity and colon cancer did not vary across subgroups of women defined by postmenopausal hormone use ($p_{interaction}$ = 0.94) or menopausal status ($p_{interaction}$ = 0.53). The association between physical activity and colon cancer also was not modified by age, BMI, total energy intake, smoking status, level of education, aspirin use, dietary intakes of fat, fiber, calcium, folate, vitamin D, red meat or alcohol (all $p_{interaction}$ > 0.05). The multivariable RRs across increasing categories of the number of times a person sweat per week showed no clear linear trend (p_{trend} = 0.56). The RRs of colon cancer among women across increasing categories of the number of times per week an individual engaged in sweat-inducing physical activity were 1.0, 1.10, 1.26, 0.97 (95% CI: 0.62, 1.54).

The results from analyses examining the association between total physical activity and colon cancer risk by anatomic subsite are given in Table III. No significant association between total, moderate or vigorous physical activity with cancer of either the proximal or distal colon was detected. The multivariable RRs of proximal colon cancer across increasing quintiles of total physical activity were 0.88, 0.96, 1.05 and 0.87 (95% CI: 0.46, 1.62; p_{trend} = 0.84). For distal colon cancer, the multivariable RR comparing women in the top to those in the bottom tertile of total physical activity (based on 68 cases) was elevated but not statistically significant (RR: 1.36; 95% CI: 0.75, 2.46). Comparing women at the extremes of moderate activity, the multivariable RR of proximal colon cancer was 1.05 (95% CI: 0.54, 2.03); for distal colon cancer, the multivariable RR was 1.10 (95% CI: 0.59, 2.07). The multivariable RRs comparing women at the extremes of vigorous physical activity were similarly null for cancer of the proximal (RR: 1.07; 95% CI: 0.63, 1.83) and distal colon (RR: 1.26; 95% CI: 0.71, 2.23).

Table III. Relative Risk (RR) of Colon Cancer in Relation to Total Physical Activity According to Anatomic Subsite in the BCDDP Follow-up Study

Proximal colon cancer[1]						*p*-trend
MET-hr/day	34.0-48.5	48.51-54.3	54.31-59.0	59.1-64.9	65.0-98.1	
Cases	23	19	21	22	18	
Person-years	52,666	53,628	54,645	55,556	53,830	
Age-adjusted RR (95% CI)	1.00	0.84 (0.46, 1.54)	0.90 (0.50, 1.63)	0.97 (0.54, 1.74)	0.97 (0.54, 1.74)	0.64
Multivariable RR (95% CI)	1.00	0.88 (0.48, 1.61)	0.96 (0.53, 1.74)	1.05 (0.58, 1.89)	0.87 (0.46, 1.62)	0.84
Distal colon cancer[2]						
MET-hr/day	34.0-52.4	52.41-60.9	61.0-98.1	N/A	N/A	
Cases	19	22	27	N/A	N/A	
Person-years	88,564	90,425	91,335	N/A	N/A	
Age-adjusted RR (95% CI)	1.00	1.13 (0.61, 2.09)	1.38 (0.77, 2.48)	N/A	N/A	0.28

Multivariable RR (95% CI)[3]	1.00	1.14 (0.76, 2.46)	1.36 (0.75, 2.46)	N/A	N/A	0.34

[1] For proximal colon cancer analysis, total physical activity was categorized in quintiles.

[2] For distal colon cancer analysis, total physical activity was categorized into tertiles due to small case numbers.

[3] Multivariable models are adjusted for age, body mass index, education, family history of colorectal cancer, smoking status, menopausal hormone use, aspirin use, alcohol consumption and energy-adjusted intakes of calcium and red meat.

Discussion

In this prospective study among US women, we did not observe an association between total, moderate or vigorous physical activities and the subsequent risk of colon cancer. Our rationale for examining the relationship between physical activity and colon cancer risk is based on several potential biologic mechanisms. Physical activity may confer protection against colon cancer by accelerating gastrointestinal transit time,[45] by upregulating immune function[46] or by altering the production of prostaglandins, insulin, insulin-like growth factors and insulin-like binding proteins.[6]

Although it seems biologically plausible that physical activity could lead to a lower risk of colon cancer, not all previous epidemiologic studies have observed an inverse association in women. Specifically, 10[19][20][23][29][30][31][32][33][34][35] out of 16[17][19][20][21][23][25][26][27][28][29][30][31][32][33][34][35] prospective studies have found no inverse association between physical activity and colon cancer in women. One possibility for the null findings on physical activity and colon cancer in women in our study and in previous studies is the potential for imprecision related to the measurement of physical activity.[36] Such imprecision would tend to limit the ability to detect a potentially weak to modest association, such as that between physical activity and colon cancer. In contrast, an imprecise measurement of physical activity may be sufficiently sensitive to uncover a potentially strong relation, such as that linking physical activity to cardiovascular disease. For example, the physical activity instrument in the Iowa Women's Health Study predicted ischemic heart disease,[47] but no association was found for colon cancer.[30] Specifically, the Iowa Women's Health Study compared women at the extremes of physical activity and reported an RR of coronary heart disease mortality of 0.7 (95% CI: 0.4, 1.1),[47] whereas the corresponding RR of colon cancer was 0.95 (95% CI: 0.70, 1.39).[30]

The physical activity instruments used in that[30] and other null studies[19][20][23][29][31][32][33][34][35] of colon cancer in women included 1,[20][33][35] 2,[29][30][31][34] 3[23] or an unspecified number[19] of broad questions that inquired about all activities simultaneously. Each of these questions allowed for 3,[29][34] 4,[31][33][35] 5[20][23] or an unspecified number[19][30] of response options. In contrast, the physical activity instruments used in 2[25][28] of 3[17][25][28] prospective studies that detected a statistically significant inverse relation of self-reported physical activity to colon cancer in women, specifically inquired about a minimum of 7 individual activities, with between 4[25] and 10[28] possible response options each. For example, by comparing women reporting greater than 21 to those reporting less than 2 MET-hr per week of recreational activity, the RR of colon cancer in the Nurses' Health Study[28] was 0.54 (95%: 0.33, 0.90). Similarly, the Cancer Prevention Study-II Nutrition Cohort[25] observed a strong reduction in colon cancer risk among women who reported engaging in 7 or more hours of recreational activities per week compared to those reporting less than 4 hr per week (RR: 0.59; 95% CI: 0.36-0.98). Notably, the earlier null report[35] from the Cancer Prevention Study-II used 1 single question encompassing all activities and did not include the level of detail that subsequently yielded a significant inverse finding[25] in that cohort.

It is worth noting that the assessments of self-reported physical activity in the 3 significant studies[17][25][28] all had documented validity. The Nurses' Health Study[28] and the Cancer Prevention Study-II Nutrition Cohort[25] used a similar instrument and the correlation between that assessment and physical activity recorded in 4 1-week diaries was 0.62.[48] Similarly, in the study by Thune and Lund,[17] a reasonable correlation was found between leisure-time activity and physical fitness.[49] In contrast, only 2[20][33] out of 10[19][20][23][29][30][31][32][33][34][35] null studies documented the validity of their assessments of self-reported physical activity. The physical activity instrument used in our study most closely resembles the one used in the Framingham Heart Study,[20] which showed a correlation between physical activity reported on

the questionnaire and that from indirect calorimetry of 0.43.[50]

Apart from potentially true differences in the metabolic response to physical activity between women and men,[51] a further possibility for the null findings of prospective studies on physical activity and colon cancer in women is the methodologically greater challenge in measuring physical activity in women as compared to that in men.[37] For example, the Framingham Heart Study[20] reported an RR of developing colon cancer of 1.1 (95% CI: 0.6, 1.8) comparing women in the lowest to those in the highest tertile of total physical activity. In the Cancer Prevention Study-II,[35] the RR of fatal colon cancer comparing women engaging in heavy exercise compared to those reporting no exercise was 0.90 (95% CI: 0.41, 1.96). In contrast, the physical activity instruments used in the Framingham Heart Study[20] and the Cancer Prevention Study-II[35] both yielded significant inverse associations for colon cancer among men in those cohorts.

The strengths of our study warrant mention. Our study's prospective design minimized the influence of colon cancer diagnosis on physical activity habits and the possibility for recall bias. In addition, the availability of information on a wide range of covariates allowed us to address possible confounding. Furthermore, in contrast to analyses of recreational activity, in which increasing education levels usually correspond to greater recreational physical activity,[52] education level was inversely related to physical activity in our dataset. This covariate pattern minimizes the possibility that our results were confounded by socioeconomic status or a healthy lifestyle.

Several limitations of our study should be considered. We used one assessment of physical activity during the preceding year as a proxy for exposure to long-term physical activity. It is possible that this physical activity measurement did not capture the etiologically relevant time period during which physical activity may confer protection against colon cancer. However, "usual" activity during the previous year has been linked to a significantly reduced risk of colon cancer in several previous studies.[17][25][28]

We were concerned about the possibility of misclassification of moderate and vigorous types of activities in our study because our examples of moderate activity contained some types of activities that are truly light activity (*e.g.*, washing clothes) and the vigorous category contained some activities that are likely moderate (*e.g.*, washing windows). Although the number of misclassified activities in our study was modest, such misclassification would tend to attenuate RR estimates because of random error in capturing and quantifying the most relevant measures of physical activity.

We were unable to quantify the validity with which activity intensity and duration were measured by our questionnaire. Roughly 58% of our study participants reported engaging in at least 30 min of vigorous activity per day. This rather high level of vigorous activity was likely due to the inclusion of numerous vigorous household activity items in our questionnaire, such as heavy housework, scrubbing floors, washing windows and heavy yardwork. Thus, our questionnaire may have overestimated the absolute amount of vigorous activity compared to previous studies that did not assess vigorous household activity. Notwithstanding, our questionnaire likely performed reasonably well in providing rankings of vigorous activity levels among women in our study. Household activity may be of particular significance in women[37] and has been included in few analyses of physical activity and colon cancer risk to date.[38]

A further alternative explanation for the lack of an association between physical activity and colon cancer among women in our study is that we inquired about the combination of recreational, occupational and household activities, and hence, could not distinguish between types of activity. In contrast, the 2 studies that reported a strong inverse relation[25][28] focused on leisure-time activity as their measure of exposure. A recent meta-analysis of physical activity and colorectal cancer combined the results of 12 cohort studies among women and reported a statistically significant decrease in the risk of colon cancer with increasing levels of recreational (combined RR: 0.72; 95% CI: 0.57, 0.89) but not occupational physical activity (combined RR: 1.12; 95% CI: 0.85, 1.47),[53] suggesting that the association of physical activity with colon cancer risk in women may differ by physical activity type.

In summary, our results do not support the hypothesis that physical activity confers significant protection against the overall development of colon cancer in women. Our findings point towards the need for conducting further research, particularly among women, that uses well-formulated, accurate measures of physical activity and distinguishes between different types of physical activity (*i.e.*, recreational, occupational, and household activity) in relation to colon cancer risk.

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